

## REMARKS

Applicants respectfully request reconsideration of the subject matter identified in caption, as amended, pursuant to and consistent with 37 C.F.R. § 1.112, and in light of the remarks which follow.

Claims 19, 20 and 23-48 are pending in the application, new Claims 38-48 have been added above.

By the above amendments, Claim 19 is amended by rearranging the order of the original wording so that the claim is easier to read. Applicants have also amended Claims 25-26 and Claims 33-34 by replacing "compound" with -- antagonist-- so that the claims are more consistent with independent Claims 19 and 20. Support for this amendment can be found at least at paragraph 38 on page 9 of the specification. Because these amendments only clarify the claims and do not narrow their scope, Applicants submit that the claims should be accorded their full range of equivalents. Finally, Applicants added new Claims 38-48 to further define exemplary embodiments of the invention. Support for new Claims 38-48 can be found at least at Claim 19.

Applicants thank the Examiner for acknowledging that the Response and Declaration filed on May 25, 2004, have overcome the 35 U.S.C. § 112, first paragraph, rejection set forth in the previous Official Action.

Additionally, Applicants thank Supervisory Examiner Padmanabhan and Examiner Yu for the courtesies extended to their representative, Martin A. Bruehs, during the personal interview conducted on October 20, 2004. In particular, Applicants thank the Examiners for indicating that the § 112, second paragraph, rejection would be withdrawn in view of the above amendments and following

remarks. Applicants also thank the Examiners for indicating that they will give favorable consideration to Applicants' position concerning the outstanding prior art rejections and newly added claims.

Turning now to the Official Action, Claims 19, 20 and 23-37 stand rejected under 35 U.S.C. § 112, second paragraph as being indefinite. For at least the reasons that follow, withdrawal of the rejection is in order.

The Official Action asserts that Claims 19 and 20 are vague and indefinite because the claims are directed to a composition comprising an agent that elicits an irritant side effect and a TNF-alpha antagonist, but that the claims also recite that the agent that elicits an irritant side effect cannot be in a composition with a TNF-alpha antagonist.

As explained during the personal interview, however, Applicants believe that upon careful consideration of the claims in their entirety, and the supporting specification, one will find that the claims point out and distinctly claim the subject matter which Applicants regard as their invention. That is, because the scope of the subject matter embraced by Claims 19 and 20 is clear, and Applicants have not otherwise indicated that they intend the claim to be of different scope, the claims particularly point out a distinctly claim the subject matter which Applicants regard as their invention. (See *In re Borkowski*, 422 F.2d 904, 164 U.S.P.Q. 642 (CCPA 1970).)

The Federal Circuit has had the opportunity to decide a number of § 112, second paragraph, cases. From these cases, it is clear that definiteness of claim language must be analyzed, not in a vacuum, but in light of (1) the content of the particular application disclosure, (2) the teachings of the prior art, and (3) the claim

interpretation that would be given by one possessing the ordinary level of skill in the pertinent art at the time the invention was made. (See, for example, *In re Marosi*, 710 F.2d 799, 218 U.S.P.Q. 289 (Fed. Cir. 1983).) The purpose of claims is not to explain the technology or how it works but to state the legal boundaries of the patent grant. The claim is not "indefinite" simply because it is hard to understand when viewed without the benefit of the specification. (See *S3, Inc. v. nVidia Corp.*, 259, F.3d 1364, 59 U.S.P.Q.2d 1745 (Fed. Cir. 2001).)

Applicants submit that the meaning of the claims is clear even when read without consideration of the supporting disclosure, teachings of the prior art or the interpretation of those possessing the ordinary level of skill in the art. Specifically, upon careful reading the claims, Applicants believe that it is clear that the claims defines a composition comprising an amount of at least one agent sufficient to elicit an irritant side effect to a user, which when used in a composition that does not include a TNF-alpha antagonist, would elicit an irritant side effect, and an amount of TNF-alpha antagonist that is sufficient to eliminate or alleviate the irritant side effect that would otherwise be elicited by the amount of the at least one irritant agent. Thus, the claim does not recite a composition "with and without a TNF-alpha antagonist." Instead, the claim is directed to a composition that includes an amount of an irritating agent, which when present in the absence of a TNF-alpha antagonist would elicit an irritant side effect, and an amount of a TNF-alpha antagonist that is sufficient to alleviate the irritant side effect that would be elicited by the irritant agent in the absence of TNF-alpha antagonist.

Applicants submit that this understanding is further supported at least by the disclosure at page 14, paragraph 57-60, which explains that exemplary

embodiments comprise a TNF-alpha antagonist and an active agent having an irritant side effect, wherein the TNF-alpha antagonist "enables this irritant effect to be greatly attenuated or even eliminated." Thus, one of ordinary skill in the art having carefully read Claims 19 and 20, and the supporting disclosure at page 14, would readily understand what the legal boundaries of Claims 19 and 20 are. That is, one of ordinary skill in the art, having read the claims in their entireties, and the supporting disclosure at page 14, would understand that the claimed compositions include both: (1) an amount of at least one agent sufficient to elicit an irritant side effect and (2) an amount of at least one TNF-alpha antagonist sufficient to eliminate or alleviate the irritant side effect.

Because one skilled in the art would be able to tell with a reasonable degree of certainty whether his or her conduct is within or outside the scope of Claims 19 and 20, the claims are neither vague nor indefinite. See *In re Borkowski*.

In order to provide further clarification of Claim 19, however, Applicants have amended Claim 19 so that the Markush group of possible active agents is recited earlier in the claim, as suggested by the Examiners during the personal interview of October 20. Since this amendment does not narrow the scope of the claims, Claim 19 should be accorded its full range of equivalents.

For at least these reasons, and in view of the Examiners' agreement to withdraw the rejection, Applicants respectfully request reconsideration and withdrawal of the § 112, second paragraph, rejection.

Claims 19-20, 23-25, 27-28, 30-33 and 35-36 stand rejected under 35 U.S.C. § 102(b) as being anticipated by Gallina (U.S. Patent No. 4,514,384). For at least the reasons that follow, withdrawal of the rejection is in order.

Independent Claim 19 defines a composition suitable for pharmaceutical, cosmetic or dermatological usage, said composition comprising:

an amount of at least one agent sufficient to elicit an irritant side-effect to a user when utilized in a composition that does not include a TNF-alpha antagonist, and wherein said irritant agent is an active agent in said composition;

an amount of at least one TNF-alpha antagonist sufficient to eliminate or alleviate said irritant side-effect; and

a cosmetically, dermatologically or pharmaceutically acceptable medium therefor wherein the agent which provides the irritant side-effect is selected from the group consisting of alpha-keto acids, beta-keto acids, retinoids, anthralins, anthranoids, peroxides, minoxidil, lithium salts, antimetabolites, vitamin D and depigmentation agents. (Emphasis added.)

Independent Claim 20 defines a composition suitable for pharmaceutical, cosmetic or dermatological usage, said composition comprising:

an amount of at least one agent sufficient to elicit an irritant side-effect to a user when utilized in a composition that does not include an interleukin-1 antagonist or a TNF-alpha antagonist, and wherein said irritant agent is an active agent in said composition;

an amount of at least one interleukin-1 antagonist and at least one TNF-alpha antagonist, sufficient to eliminate or alleviate said irritant side-effect; and

a cosmetically, dermatologically or pharmaceutically acceptable medium therefor. (Emphasis added.)

Gallina relates to an improved method of hemorrhoid treatment by use of a preparation containing either urea hydrogen peroxide or benzoyl peroxide in

combination with hydrocortisone for producing a cleansing, debriding, keratolytic, antiseptic, anti-inflammatory, vasoconstrictive, antipruritic, re-epithelization and healing action on rectal tissues. (See Gallina at Col. 1, lines 42-51.)

The Official Action takes the position that Gallina exemplifies a composition comprising an effective amount of an agent to elicit an irritant side effect (10% benzoyl peroxide) and an amount of IL-1 and TNF-alpha antagonist sufficient to eliminate or alleviate the irritant side effect (i.e., 1% hydrocortisone alcohol). (See Official Action at page 3.)

It is well-established that in order to demonstrate anticipation under § 102(b) each element of the claim and issue must be found, either expressly described or under principles of inherency, and a single prior art reference. See Kalman v. Kimberley-Clark Corp., 218 U.S.P.Q. 789 (Fed. Cir. 1983). That is not the case here.

In particular, Applicants submit that Gallina does not indicate that hydrocortisone alcohol is a TNF-alpha antagonist or an IL-1 and TNF-alpha antagonist, as recited in Claims 19 and 20, respectively. Accordingly, Applicants submit that Gallina does not expressly or inherently disclose these elements of Claims 19 and 20.

For at least these reasons, Claims 19 and 20 are patentable over Gallina. Because the remaining claims (i.e., Claims 23-25, 27-28, 30-33 and 35-36) depend, either directly or indirectly from independent Claims 19 and 20, these claims are also patentable over Gallina for at least the reasons that Claims 19 and 20 are patentable. Applicants respectfully request reconsideration and withdrawal of the rejection.

Claims 26 and 34 stand rejected under 35 U.S.C. § 103(a) over Gallina, and further in view of Dubash (U.S. Patent No. 4,383,986). For at least the reasons that follow, withdrawal of the rejection is in order.

The Official Action asserts that Dubach teaches hemorrhoid compositions comprising hydrocortisone as active ingredients, wherein 0.001-0.5% is taught as a therapeutically effective amount of hydrocortisone. Thus, the Official Action asserts that it would have been obvious to one of ordinary skill in the art at the time the invention was made to teach the hydrocortisone of Gallina as comprising 0.001-0.1% of the composition, as taught by Dubash because both are directed toward compositions comprising hydrocortisone as active ingredients for treating hemorrhoids, because Dubash teaches 0.001-0.1% as a therapeutically effective amount of hydrocortisone for the treatment of hemorrhoids and because it has been held that where the general conditions of a claim are disclosed in the art, discovering the optimum or workable ranges involves only routine skill in the art. (See Official Action at page 4.)

To establish a *prima facie* case of obviousness, the prior art references (or references when combined) must teach or suggest all of the claim elements. See *In re Royka*, 490 F.2d 981, 180 U.S.P.Q. 580 (CCPA 1974). In addition, "all words in a claim must be considered in judging the patentability of that claim against the prior art." See *In re Wilson*, 424 F.2d 1382, 1385; 165 U.S.P.Q. 494, 496 (CCPA 1970). See MPEP § 2143.03.

First, as explained above, Applicants submit that Gallina does not disclose or suggest that hydrocortisone is a TNF-alpha antagonist or an IL-1 and TNF-alpha antagonist, as recited in Claims 19 and 20, respectively. Similarly, Dubash fails to

disclose or suggest that hydrocortisone is a TNF-alpha antagonist or an IL-1 and TNF-alpha antagonist. Accordingly, Applicants submit that the combination of Gallina in view of Dubash does not render the subject matter of Claims 26 and 34 obvious because the combination does not disclose or fairly suggest a TNF-alpha antagonist or an IL-1 and TNF-alpha antagonist, as recited in independent Claims 19 and 20, from which Claims 26 and 34 depend, respectively,

The asserted combination also fails to reflect a proper consideration of "all words" in Claims 19 and 20, from which Claims 26 and 34 depend, respectively, because neither of the references alone or in combination, disclose or suggest a composition comprising an amount of a TNF-alpha antagonist or an amount of IL-1 and TNF-alpha antagonist, sufficient to eliminate or alleviate an irritant side effect. In particular, because the asserted combination does not disclose or suggest such a composition, Applicants submit that the Official Action has not given full consideration to all claimed elements, i.e., patentable weight must be given to "an amount of at least one TNF-alpha antagonist sufficient to eliminate or alleviate said irritant side effect," and "an amount of at least one interleukin-1 antagonist and at least one TNF-alpha antagonist, sufficient to eliminate or alleviate said irritant side effect," as recited in independent Claims 19 and 20, respectively, in judging the patentability of Claims 26 and 34 over the asserted combination.

In addition, Applicants submit that because the asserted combination of references fails to even consider the problem of eliminating or alleviating an irritant side effect elicited by an active agent provided in a cosmetically, dermatologically or pharmaceutically acceptable medium, as recited in independent Claims 19 and 20,

from which Claims 26 and 34 depend, respectively, the claimed compositions would not have been obvious over the asserted combination of references.

That is, while the claimed compositions are defined to include an amount of at least one TNF-alpha antagonist or an amount of least one interleukin-1 antagonist and at least one TNF-alpha antagonist, sufficient to eliminate or alleviate said irritant side effect, the cited references are directed entirely to the treatment of hemorrhoids. Thus, Applicants submit that the combination of references are not relevant to the use of an effective amount of a TNF-alpha antagonist or an effective amount of an IL-1 and TNF-alpha antagonist sufficient to eliminate or alleviate an irritant side effect elicited by an active agent in a composition provided in a cosmetically, dermatologically or pharmaceutically acceptable medium.

Applicants submit that the Official Action also fails to establish that the prior art provides a reasonable expectation of success. In particular, MPEP § 2143.02 states that a reasonable expectation of success is required to establish a *prima facie* case of obviousness. That is, beyond looking to the prior art to determine if it suggests doing what the inventor has done, one must also consider if the art provides the required expectation of succeeding in that endeavor. (See In re Dow Chem. Co. v. American Cyanamid, 837 F.2d 473, 5 U.S.P.Q.2d at 1531 (both the suggestion and expectation of success must be founded in the prior art, not in Appellants disclosure).) In this case, however, the asserted combination of references provides neither a suggestion nor an expectation of success in doing what the inventors have done (i.e., combining a amount of at least one agent sufficient to elicit an irritant side effect with an amount of at least TNF-alpha antagonist or interleukin-1 antagonist and TNF-alpha antagonist, sufficient to

eliminate or alleviate said irritant side effect). Specifically, one would not have expected to obtain the claimed compositions by combining and modifying compositions that include hydrocortisone taught for use in the treatment of hemorrhoids to arrive at the claimed compositions.

For at least the above reasons, Claims 26 and 34 are patentable over the combination of Gallina in view of Dubash. Applicants respectfully request reconsideration and withdrawal of the rejection.

Claims 28 and 37 stand rejected under 35 U.S.C. § 103(a) as being unpatentable over Gallina, further in view of Allen (U.S. Patent No. 4,895,727). For at least the reasons that follow, withdrawal of the rejection is in order.

The Official Action asserts that Gallina teaches that lidocaine is taught as a topical anesthetic that can be added to the disclosed composition but that the reference lacks lidocaine hydrochloride. The Official Action further asserts that the Allen teaches lidocaine and lidocaine hydrochloride as equivalent anesthetic agents. Accordingly, the Official Action asserts that it would have been obvious to teach the lidocaine of Gallina and lidocaine hydrochloride, as taught by Allen, because of the expectation of achieving equivalent anesthetics. (See Official Action at pages 4-5.)

As explained above, however, to establish a *prima facie* case of obviousness, the prior art references (or references when combined) must teach or suggest all of the claim elements and all "all words in a claim must be considered in judging the patentability of that claim against the prior art." See *In re Royka*; *In re Wilson*; and MPEP § 22143.03.

Gallina does not disclose or suggest that hydrocortisone is a TNF-alpha antagonist or an IL-1 and TNF-alpha antagonist, as recited in independent Claims 19

and 20, from which Claims 29 and 37 depend. Moreover, Applicants submit that Allen does not overcome this deficiency. Accordingly, Applicants submit that the combination of Gallina further in view of Allen does not establish a *prima facie* case of obviousness because it does not disclose or fairly suggest all of the elements of Claims 19 and 20, from which Claims 29 and 37 depend.

Additionally, the asserted combination does not reflect a proper consideration of "all words" in Claims 19 and 20, from which Claims 29 and 37 depend. In particular, because the asserted combination does not disclose or fairly suggest a composition comprising an amount of at least one TNF-alpha antagonist or an amount of an IL-1 and TNF-alpha antagonist sufficient to eliminate or alleviate an irritant side effect, Applicants submit that the Official Action has not given full consideration to all claimed elements i.e., patentable weight must be given to "an amount of at least one TNF-alpha antagonist sufficient to eliminate or alleviate said irritant side effect," and "an amount of at least one interleukin-1 antagonist and at least one TNF-alpha antagonist, sufficient to eliminate or alleviate said irritant side effect," in Claims 19 and 20, in judging the patentability of Claims 29 and 37 over the asserted combination.

In addition, Applicants submit that because the asserted combination of references fails to even consider the problem of eliminating or alleviating said irritant side effect elicited by an amount of active agent in a composition suitable for pharmaceutical, cosmetically or dermatological use, by providing an effective amount of at least one TNF-alpha antagonist or an IL-1 and TNF-alpha antagonist, the claimed compositions would not have been obvious over the asserted combinations of references.

That is, while the claimed composition provides elimination or alleviation of an irritant side effect elicited by an amount of at least one active agent by providing a effective amount of least one TNF-alpha antagonist or interleukin-1 antagonist and TNF-alpha antagonist, nowhere does the asserted combination of references disclose or suggest a solution to this problem, let alone the solution set forth in pending Claims 19 and 20, from which Claims 29 and 37 depend.

Because the asserted combination of references is entirely unrelated to eliminating or alleviating the irritant side effect elicited by an active agent in a composition suitable for pharmaceutical, cosmetically or dermatological use with a TNF-alpha antagonist or an IL-1 and TNF-alpha antagonist, Applicants respectfully submit that the claimed compositions would not have been obvious over the asserted combination of references.

The Official Action also fails to establish that the prior art provides a reasonable expectation of success. As explained above, beyond looking to the prior art to determine if it suggests doing what an inventor has done, one must also consider if the art provides the required expectation of succeeding in that endeavor. (See *In re Dow Chem. Co., v. American Cyanamid*, 837 F.2d 473, 5 U.S.P.Q.2d at 1531 (both the suggestion and expectation of success must be founded in the prior art not in Applicants disclosure.)) In this case, the asserted combination of references provides neither a suggestion nor expectation of success in doing what the inventors have done (i.e., combining an active agent sufficient to elicit an irritant side effect and an effective amount of least one TNF-alpha antagonist or interleukin-1 antagonist and TNF-alpha antagonist, sufficient to eliminate or alleviate said irritant side effect). One would not have expected to obtain the claimed compositions by

combining a reference directed to a method for inducing a reservoir effect of the skin and mucous membranes to enhance penetration and retention of topically applied agents and a method for treating hemorrhoids with a peroxide and hydrocortisone to arrive at a composition suitable for pharmaceutical, cosmetically or dermatological use, which includes both: (1) an amount of active agent that elicits an irritant side effect and (2) an effective amount of least one TNF-alpha antagonist or interleukin-1 antagonist and TNF-alpha antagonist to eliminate or alleviate said irritant side effect.

For at least these reasons, Applicants submit that Claims 29 and 37 are patentable over the combination of Gallina in view of Allen. Accordingly, Applicants respectfully request reconsideration and withdrawal of the rejection.

Finally, Applicants have added new Claims 38-48 to further define exemplary embodiments of the invention. Applicants submit that these claims are also patentable over the cited prior art references for at least the reasons stated above. In addition, Applicants submit that new Claims 38-42 and 44-48 are further distinguished from Gallina, Dubash and Allen, alone or in combination, because these claims recite active agents other than a peroxide, as required by Gallina.

From the foregoing, Applicants earnestly solicit further and favorable action in the form of a Notice of Allowance.

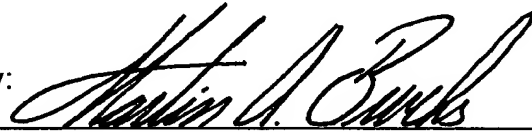
If there are any questions concerning this paper or the application in general,  
Applicants invite the Examiner to telephone the undersigned at the Examiner's  
earliest convenience.

Respectfully submitted,

BURNS, DOANE, SWECKER & MATHIS, L.L.P.

Date: October 27, 2004

By:

A handwritten signature in black ink, appearing to read "Martin A. Bruehs", written over a horizontal line.

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